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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/756,761	01/14/2004	Laurence S. Harbige	604-706	1504

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/756,761	HARBIGE ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-11 and 13-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-3,6-11,13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to Applicant's amendment received on 04/02/2008, wherein claim 1 has been amended, and claim 12 has been cancelled.

Claims 1-3, 6-11, and 13-15 are examined herein, insofar as they read on the elected invention.

Applicant's arguments have been considered, but not found persuasive. The rejection of claims 1-3, 6-9, 11, and 15 under 35 U.S.C. 102(b) as being anticipated by Lunardi et al. (Neurology, volume 48(6), 1997, pages 1714-1717, PTO-892) is MAINTAINED. See under response to arguments.

Applicant's arguments have been considered, but not found persuasive. The rejection of claims 1-3, 6-9, 11, and 13 under 35 U.S.C. 102(b) as being anticipated by Bountra et al. (WO 00/61231, PTO-1449) is MAINTAINED. See under response to arguments.

Applicant's arguments have been considered, but not found persuasive. The rejection of claims 10, 14-15 under 35 U.S.C. § 103(a) as being unpatentable over Bountra et al. (WO 00/61231, PTO-1449) is MAINTAINED. See under response to arguments.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 8-11, 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation wherein Y1 and Y2 are selected from "secondary amino groups" in claim 1 is vague and indefinite, as it is not clear what compounds this term encompasses, and since one of ordinary skill in the art could not ascertain the metes and bounds as to "secondary amino groups". The specification merely recites that preferably Y1 is selected from "- 1-piperazinyl and 4-alkyl- 1-piperazinyl ". See page 4, line 15-16. However, it is not clear what other compounds are encompassed by these terms because seconday amines have two organic substituents attached to N together with one hydrogen, and thus it is not clear what kind of substituents are attached to the N in case of secondary amino groups.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6-9, 11, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Lunardi et al. (Neurology, volume 48(6), 1997, pages 1714-1717, PTO-892).

Lunardi et al. discloses administration of lamotrigine to patients suffering from multiple sclerosis in which trigeminal neuralgia was also present. See abstract; page 1715. Lamotrigine was administered at an initial dosage of 25 mg/day, increasing in increments of 25 mg every third day up to a maximum absolute dosage of 400 mg/day. See page 1716, left hand column. Administration of lamotrigine to patients suffering from multiple sclerosis concomitant with trigeminal neuralgia resulted in complete pain relief.

It is pointed out that Lunardi et al. method inherently treats multiple sclerosis, since the method steps are same as the instant method steps, administering the same compound in the same effective amount to the same or overlapping patient population will cause the same effect, whether or not that effect is specifically disclosed by the prior art.

Further, regarding the recitations, "wherein the therapy results in reduction of one or more of incidence of relapse, spasticity and fatigue", "wherein the therapy stabilizes the patients Expanded Disability Status Score, thus halting progress of the disease", in claims 8-9, Lunardi et al. method inherently results in reduction of one or more of incidence of relapse, spasticity and fatigue", inherently halts progress of the disease, as claimed herein since Lunardi's method steps are same as the instant method steps, administering the same compound in the same amount to a patient suffering from multiple sclerosis. See *Ex parte Novitski*, 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d

1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein.

Thus, Lunardi et al. anticipates instant Claims 1-3, 6-9, 11, and 15.

Response to Arguments

Applicant argues that "Lunardi specifies a maximum dose of 400 mg/day (see abstract and Table on page 1715). None of the patients with multiple sclerosis were given this dose (see page 1715, column 1, lines 1 to 5 where these patients are identified as numbered 16 to 20 in the table). The maximum dose given to multiple sclerosis patients was 125mg/day." These arguments have been considered, but not found persuasive. Lunardi discloses that Lamotrigine was administered at an initial dosage of 25 mg/day, increasing in increments of 25 mg every third day up to a maximum absolute dosage of 400 mg/day. See page 1716, left hand column. Administration of lamotrigine to patients suffering from multiple sclerosis concomitant with trigeminal neuralgia resulted in complete pain relief. Accordingly, Lunardi clearly teaches administration of 400 mg/day of lamotrigine to patients suffering from multiple sclerosis, and thus meets the instant dose between 400 mg/day to 700 mg/day.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6-9, 11, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Bountra et al. (WO 00/61231, PTO-1449).

Bountra et al. discloses a method of treating multiple sclerosis comprising administering sodium channel antagonists such as 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine called lamotrigine, 5-amino-6-[2,3,5-trichlorophenyl]-1,2,4-triazine. See page 7, lines 20-24; page 8, lines 5-10. A dose range of 200 mg/day to 900 mg/day for an adult human is disclosed. See page 10, lines 1-8.

Regarding the recitations, "wherein the therapy results in reduction of one or more of incidence of relapse, spasticity and fatigue", "wherein the therapy stabilizes the patients Expanded Disability Status Score, thus halting progress of the disease", in claims 8-9, Bountra et al. method inherently results in reduction of one or more of incidence of relapse, spasticity and fatigue", inherently halts progress of the disease, as claimed herein since Bountra's method steps are same as the instant method steps, administering the same compound in the same amount to a patient for treating multiple sclerosis. See *Ex parte Novitski*, 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). See also *Eli Lilly and Co. v. Barr Laboratories Inc.* 251 F3d. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it related to the claimed invention herein.

Thus, Bountra et al. anticipates instant Claims 1-3, 6-9, 11, 13.

Response to Arguments

Applicant argues that "Bountra likewise contains no disclosure of the invention as claimed. Bountra proposes that sodium channel antagonists may be used to treat

neuronal apoptosis. This is irrelevant to multiple sclerosis (MS), as it is well evidenced in the art that this mechanism is not significant in that disease." These arguments, and the papers cited by the applicant have been considered, but not found persuasive. Bountra et al. clearly discloses that sodium channel antagonists are used for treating multiple sclerosis. See page 14, claim 7 of Bountre et al.; page 7, lines 20-24; page 8, lines 5-10.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10, 14-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bountra et al. (WO 00/61231, PTO-1449) as applied to claims 1-3, 6-9, 11, 13.

Bountra et al. discloses a method of treating multiple sclerosis comprising administering sodium channel antagonists such as 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine called lamotrigine, 5-amino-6-[2,3,5-trichlorophenyl]-1,2,4-triazine. See page 7, lines 20-24; page 8, lines 5-10. A dose range of 200 mg/day to 900 mg/day for an adult human is disclosed. Bountra et al. also teaches that it may be necessary to make routine variation to the dosage, depending on the age and condition of the patient. See page 10, lines 1-8.

Bountra et al. does not specifically teach the amount of lamotrigine as 600 mg/day as in claim 14, and the dosing regimen as in claim 15.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as effective amounts of lamotrigine to be administered in the method of treating multiple sclerosis.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of lamotrigine employed in the method of treating multiple sclerosis, since the optimization of effective amounts of known agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of known ingredients in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

One of ordinary skill in the art at the time of invention would have been motivated to the particular treatment regimen because the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in the art.

Response to Arguments

Applicant argues that "Bountra does not render the present invention obvious. Bountra provides no credible guidance on how to dose and what to dose. A person of ordinary skill in the art might easily have selected carbamazepine, as did Ramsaransing

et al, and then dose at 900mg with serious detrimental effect." These arguments have been considered, but not found persuasive. Bountra et al. clearly discloses the use of a sodium channel antagonists such as 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine called lamotrigine, 5-amino-6-[2,3,5-trichlorophenyl]-1,2,4-triazine for the treatment of multiple sclerosis. See page 7, lines 20-24; page 8, lines 5-10. Bountra et al. teaches that the sodium channel antagonists therein are employed in dose range of 200 mg/day to 900 mg/day for an adult human, and it may be necessary to make routine variation to the dosage, depending on the age and condition of the patient. One of ordinary skill in the art at the time of invention would have been motivated to the particular treatment regimen because the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in the art.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period, will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Thursday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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